UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/656,873	09/05/2003	Mark C. Fishman	00786/381003	8749

21559 7590 01/29/2009

CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
01/29/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/656,873	FISHMAN ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,8-19,21,22,33 and 34* is/are pending in the application.

4a) Of the above claim(s) *8-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,21,22,33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 1-3, 8-19, 21-22 and 33-34 re pending in the instant application. Claims 8-19 are withdrawn from consideration as being drawn to non elected inventions. Claims 1-3, 21-22 and newly added claims 33-34 are currently under examination. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. The following rejections are either newly applied, as necessitated by amendment, or are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.

2. The rejections under 35 USC 112/first paragraph, made in the previous office action are withdrawn in view of the amendments to the claims to recite a method of screening for mutations in the titin gene in humans which may indicate that the etiology of heart failure in the human subject may relate to the mutation, and in view of applicants arguments. At page 7, applicants argue that the claims now are directed such that: "if there is not a mutation in the test sequence, a mutation cannot be related to the etiology of the heart failure, while if there is a mutation, there may be a relationship between the mutation and the subject's condition, which is a matter that could be studied further, if desired. " (response, pages 6-7) Accordingly, the claims are directed to screening for mutations in the titin gene in human individuals. The recitation of "may indicate" allows for methods which detect mutations, but which "may not" indicate the etiology of heart failure, however such methods would still read on the claim.

3. Claim 1 has been amended to recite SEQ ID NO: 2 which was not submitted in the provisional application 60/175,787, filed 1/12/2000. Accordingly, the effective filing date of the instantly pending claims is 1/12/2001.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-3, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Satoh et al (Biochemical and Biophysical Research Communications, vol. 262, pp 411-417, 1999).

With regard to claims 1, and 21, Satoh teaches of an A to T transversion in codon 740 of the titin gene of a human patient with hypertrophic cardiomyopathy, which replaces an Arginine with Leucine (see abstract). Satoh teaches that this mutation was not found in more than 500 normal chromosomes (see abstract). With regard to claims 2, 3, Satoh teaches that genomic DNA was extracted from each subject and that PCR primers flanking each exon of the titin gene were designed to amplify each exon (p. 412-col. 1, "PCR-DCP analysis") and that to identify the mutation in exon 14, the PCR product was cloned into a vector and sequenced (para. bridging cols 1 and 2, p. 412). With regard to comparison to SEQ ID NO: 2, Satoh teaches comparison to human titin amino acid sequence (see figure 3, and page 412, col 2 "amino acid sequence alignment…", including recitation of Genbank Accession number X90568). Accordingly, the teachings of Satoh anticipate the claims.

Response to Arguments

6. The response requests that the rejection be withdrawn in view of an accompanying Declaration under 37 CFR 1.131 by inventors Mark Fishman and Xialei Xu. It is noted, however, that the instant rejection is set forth under 35 USC 102(b), and therefore a declaration under 37 CFR 1.131 cannot be used to overcome the rejection. Further, should the claims be awarded the benefit of the '787 provisional application, the declaration is insufficient to overcome a rejection under 35 USC 102(a) as the claims now require analysis in a human subject and comparison to at least a portion of SEQ ID NO: 2. In contrast, the declaration only shows analysis in zebrafish and is entirely silent as to the sequence of SEQ ID NO: 2. Accordingly, there is no overlap between the scope of the instantly claimed invention and that shown in the declaration The guidance provided in the MPEP states as follows:

MPEP 715.02 [R-6] "How Much of the Claimed Invention Must Be Shown, Including the General Rule as to Generic Claims"

The 37 CFR 1.131 affidavit or declaration must establish possession of either the whole invention claimed or something falling within the claim (such as a species of a claimed genus), in the sense that the claim as a whole reads on it. In re Tanczyn, 347 F.2d 830, 146 USPQ 298 (CCPA 1965)

Accordingly, the rejection is maintained as anticipated over the teachings of Satoh and newly applied under 35 USC 102(b) in view of the amendments to the claims.

7. Claims 1-3, 21-22 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Siu (Siu et al Circulation, vol 99, pages 1022-1026, March 2, 1999).

With regard to claims 1-3 and 21-22, Siu teaches a method of obtaining a nucleic acid containing sample from a human test subject, including subject's with congestive heart failure

(claim 33, see page 1024), and amplifying a naturally occurring cardiac specific N2B exon of human titin gene sequence to determine it's sequence. It is noted that claim 1, recites comparison with SEQ ID NO: 2, however the claim does not require comparison to the entire sequence, nor does the specification recite such. The specification does teach that comparison can be made with SEQ ID NO: 2, however, again, no requirement is made that comparison is made to the entire sequence. Further, claim 3 recites "wherein analyzing of said nucleic acid molecule comprises sequencing titn nucleic acid molecules". The specification defines "titin nucleic acid molecules" (page 3) as genomic DNA, cDNA or RNA molecule that encodes titin, a tin protein, a titin polypeptide *or a portion thereof.* Accordingly, the claims have been given their broadest reasonable interpretation in light of the teachings of the specification, to encompass comparison to a portion of SEQ ID NO: 2. Siu teaches that nucleotide sequence was determined and compared to titin cDNA sequences. Siu teaches detecting 2 mutations which predicted the substitution of a threonine to a proline, and a leucine to a phenylalanine. Accordingly, the teachings of Siu anticipate claims 1-3, 21-22, and 33.

Response to Arguments

8. The response traverses the rejection and asserts that the claims have been amended to recite detection of a mutation. This argument has been thoroughly reviewed but was not found persuasive as Siu also teaches detection of mutations in the human titin gene. It should be noted, however, that the claim still recites "analyzing… to determine whether the test subject has a mutation". This does not require detection of a mutation. The "wherein" clause does not appear to require detection of a mutation, rather specifies that analysis is carried out by comparison to SEQ ID NO: 2, such that if any mutation is present, it would be detected by the comparison.

Claim Rejections - 35 USC § 103

9. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Satoh.

Satoh teaches of an A to T transversion in codon 740 of the titin gene of a human patient with hypertrophic cardiomyopathy, which replaces an Arginine with Leucine (see abstract). Satoh teaches that this mutation was not found in more than 500 normal chromosomes (see abstract). Satoh teaches that although a study which looked at 1000 amino acids of the N2B region of human titin did not find an association between mutations and DCM, the N2B region is 27000 amino acids long and the entire region should be analyzed. Satoh teaches that such analysis is being performed. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to analyze the N2B region of titin in a population of test subjects as Satoh teaches to do so with a reasonable expectation of success, as mutations have been found in that region as taught by Satoh.

10. Claims 33 and 34 are rejected over Satoh in view of Wagoner (Wagoner et al; Current opinion in cardiology, (1996 May) Vol. 11, No. 3, abstract).

Satoh teaches of an A to T transversion in codon 740 of the titin gene of a human patient with hypertrophic cardiomyopathy, which replaces an Arginine with Leucine (see abstract). Satoh teaches that this mutation was not found in more than 500 normal chromosomes (see abstract). Satoh teaches that the mutation affects the interaction of titin with a-actin (page 414). Satoh teaches that although a study which looked at 1000 amino acids of the N2B region of human titin did not find an association between mutations and DCM, the N2B region is 27000 amino acids long and the entire region should be analyzed. Satoh teaches that such analysis is being performed in patients with DCM and HCM. Satoh does not specifically teach such

analysis in patients with congestive heart failure or patients with low output heart failure, however Wagoner discusses the relationship between congestive heart failure, hypertrophy and contractile failure, and low output heart failure. Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to perform the studies taught by Satoh, in patients with congestive heart failure and low output heart failure, given the art accepted relationship between hypertrophy and congestive heart failure as well as contractile failure and low output heart failure, as taught by Wagoner, with a reasonable expectation of success.

Conclusion

11. No claims are allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday, Tuesday and Thursday from 9:00 AM to 3:00 PM.

NOTE: The examiner will be on Maternity Leave May through August 2009.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Jehanne Sitton/
Primary Examiner
Art Unit 1634